(220 mg, 72%) as a gum: IR ($CHCl_3$) 3400, 1742, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.10 (q, J = 7 Hz, 2 H, OCH_2CH_3), 4.35 (d, J = 2 Hz, 1 H, C_4-H), 5.20 (s, 2 H, CH_2Ph), 7.40 (s, 5 H, Ar H).

Mesylate 22. A solution of the azetidinone **21** (50 mg, 0.13 mmol), triethylamine (0.02 mL, 0.14 mmol), and methanesulfonyl chloride (0.1 mL, 0.13 mmol) in methylene chloride (5 mL) was stirred at ambient temperature for 2 h under a current of nitrogen. After the mixture had been diluted with methylene chloride (50 mL), the organic layer was separated, washed with brine, dried over sodium sulfate, and concentrated to leave the residue, which was subjected to column chromatography on silica gel. Elution with benzene–ethyl acetate (95:5 v/v) provided the mesylate **22** (42 mg, 69.6%) as a gum: IR ($CHCl_3$) 3400, 1773, 1726 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.15 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.72 (q, J = 7 Hz, 2 H, $C_3CH_2CH_3$), 3.20 (s, 3 H, SO_2CH_3), 4.00 (q, J = 7 Hz, 2 H, OCH_2CH_3), 4.22 (d, J = 2 Hz, 1 H, C_4H), 5.10 (s, 2 H, CH_2Ph), 7.24 (s, 5 H, Ar H).

Phosphonate 23. A solution of the azetidinone **21** (150 mg, 0.4 mmol), diisopropylethylamine (0.075 mL, 0.42 mmol), and diphenylphosphonyl chloride (107 mg, 0.4 mmol) in dry methylene chloride (10 mL) was stirred at 0 °C for 3 h under a current of nitrogen. After the mixture was diluted with methylene chloride (50 mL), the organic layer was separated, washed with brine, dried over sodium sulfate, and concentrated to give the residue, which was chromatographed on silica gel with benzene–ethyl acetate (98:2 v/v) as eluant to afford the phosphonate **23** (168 mg, 69.7%) as a gum: IR ($CHCl_3$) 3410, 1770, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.24 (t, J = 7 Hz, 3 H, CH_2CH_2), 4.15 (q, J = 7 Hz, 2 H, OCH_2CH_3), 4.45 (d, J = 2 Hz, 1 H, C_4H), 5.07 (s, 2 H, CH_2Ph), 6.50 (s, 1 H, NH), 7.1–7.5 (m, 15 H, Ar H).

Reaction of 19 with Acetyl Chloride. To a stirred solution of lithium hexamethyldisilazide [prepared from hexamethyldisilazane (2.5 mL, 11.7 mmol) and 15% solution of *n*-butyllithium in *n*-hexane (4.6 mL, 10.7 mmol)] in dry tetrahydrofuran (30 mL) was added a solution of the azetidinone **19** (1.7 g, 5.1 mmol) in dry tetrahydrofuran (15 mL) at −78 °C under a current of nitrogen. After the mixture was stirred for 0.2 h at −78 °C, acetyl chloride (0.38 mL, 5.1 mmol) was added to the above solution, and the resulting mixture was further stirred for 0.5 h at −78 °C. The mixture was treated with 10% aqueous acetic acid and extracted with methylene chloride. The organic extract was washed with brine and dried over sodium sulfate. Evaporation of the solvent gave the residue, which was chromatographed on silica gel using benzene–ethyl acetate (98:2 v/v) as eluant to furnish **24** (1.2 g, 63.2%) as a gum: IR ($CHCl_3$) 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.32 (s, 3 H, CH_3), 0.35 (s, 3 H, CH_3), 1.05 (s, 9 H, *t*-Bu), 2.41 (s, 3 H, olefinic CH_3), 4.28 (d, J = 2 Hz, 1 H, C_4H), 4.30 (q, J = 7 Hz, 2 H, OCH_2CH_3); mass spectrum, m/z 374 (M^+ + 1).

(±)-1-Acetyl-4-[((ethoxycarbonyl)methyl)thio]-3-ethyl-2-azetidinone (25). A. To a stirred solution of the azetidinone **24** (110 mg, 0.29 mmol) in tetrahydrofuran (10 mL) was added tetrabutylammonium fluoride (1 mmol solution in tetrahydrofuran, 0.29 mL) at ambient temperature. After the mixture was stirred for 0.5 h, the solvent was evaporated to give the residue, which was subjected to column chromatography on silica gel. Elution with benzene–ethyl acetate (95:5 v/v) afforded 25 (76 mg, 99.3%) as a gum: IR ($CHCl_3$) 1795, 1730, 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.26 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.72 (q, J = 7 Hz, 2 H, $C_3CH_2CH_3$), 2.33 (s, 3 H, $COCH_3$), 2.96 (dt, J = 2, 7 Hz, 1 H, C_3H), 3.26 (d, J = 15 Hz, 1 H, $SCHHCO$), 3.91 (d, J = 15 Hz, 1 H, $SCHHCO$), 4.04 (q, J = 7 Hz, 2 H, OCH_2CH_3), 4.89 (d, J = 2 Hz, 1 H, C_4H); mass spectrum, m/z 259 (M^+).

B. A mixture of the azetidinone **18** (50 mg, 0.23 mmol), 4-(dimethylamino)pyridine (31 mg, 0.25 mmol), acetic anhydride (25 mg, 0.24 mmol), and methylene chloride (5 mL) was stirred at room temperature of 0.5 h. After evaporation of the solvent, the residue was chromatographed on silica gel with benzene–ethyl acetate (95:5 v/v) as eluant to yield the N-acetylated azetidinone **25**, which was identical with the authentic specimen obtained above in all respects.

Acknowledgment. We thank T. Ogata, M. Yuyama, T. Tanaka, M. Moriki, and H. Furuyama of Hoshi University of spectral measurements, microanlyses, and manuscript preparation.

Practical Synthesis of (*R*)- or (*S*)-2,2′-Bis(diarylphosphino)-1,1′-binaphthyls (BINAPs)

Hidemasa Takaya,* Kazushi Mashima, and Kinko Koyano

Chemical Materials Center, Institute for Molecular Science, Okazaki National Research Institutes, Okazaki 444, Japan

Misao Yagi, Hidenori Kumobayashi, Takanao Taketomi, and Susumu Akutagawa*

Central Research Laboratory, Takasago Perfumery Co., Ltd., Kamata, Ohta-ku, Tokyo 144, Japan

Ryoji Noyori*

Department of Chemistry, Nagoya University, Chikusa, Nagoya 464, Japan

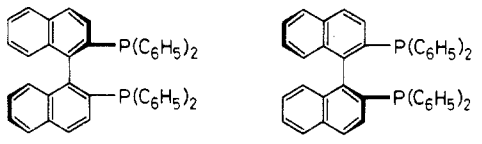
Received June 12, 1985

Practical methods for the synthesis of (*R*)- or (*S*)-2,2′-bis(diarylphosphino)-1,1′-binaphthyls (BINAPs), useful ligands for transition-metal-catalyzed asymmetric reactions, have been developed. (±)-2,2′-Bis(diphenylphosphinyl)-1,1′-binaphthyl [(±)-BINAPO], prepared from 2,2′-dibromo-1,1′-binaphthyl and diphenylphosphinyl chloride, can be resolved into optical antipodes by the use of camphorsulfonic acid or 2,3-di-*O*-benzoyltartaric acid. Reduction of resolved BINAPO with trichlorosilane in the presence of triethylamine affords optically pure 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP). In a similar manner, several BINAP analogues have been prepared in optically pure form. The present procedures are suitable for obtaining these axially dissymmetric diphosphines in a large scale. The molecular structure of the 1:1:1 complex of (*S*)-(−)-BINAPO, (1*R*)-(−)-camphorsulfonic acid, and acetic acid has been studied by single-crystal X-ray analysis.

Recently numerous chiral di-*tert*-phosphines have been devised as ligands for transition-metal-catalyzed asymmetric syntheses in the homogeneous phase.[1] Some years ago, we reported (*R*)- or (*S*)-2,2′-bis(diphenyl-

0022-3263/86/1951-0629$01.50/0

phosphino)-1,1′-binaphthyl (1) (abbreviated to BINAP),[2,3] a new atropisomeric bis(triaryl)phosphine. By virtue of

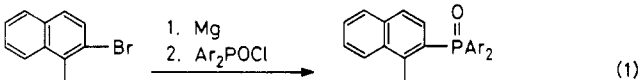


(R)-(+)-1 [(R)-BINAP] (S)-(−)-1 [(S)-BINAP]

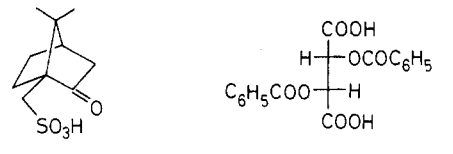
the C_2 chirality, molecular pliancy, and electronic characteristics,[4] BINAP exhibits excellent chiral recognition ability in various asymmetric reactions and is now becoming, among others, one of the most important phosphine ligands. The BINAP-coordinated Rh(I) complexes have been shown to be efficient catalysts for asymmetric hydrogenations of α-acylaminoacrylic acids[2,3] and allylic alcohols.[5] Furthermore, the chiral complexes effect a remarkable enantioselective 1,3-hydrogen shift of allylamines to optically active enamines,[6] which plays a key role in the recently established industrial synthesis of (−)-menthol. In addition, the unique features of BINAP ligands[4] also provide advantages in examining mechanisms of transition-metal-catalyzed reactions. We initially obtained this useful diphosphine ligand, (*R*)-, or (*S*)-**1**, by synthesis of racemic **1** followed by optical resolution with (+)-bis(μ-chloro)bis[(*S*)-*N*,*N*-dimethyl-1-phenylethylamine-2*C*,*N*]dipalladium(II).[2,3] Recently Murdoch[7] reported the stereospecific synthesis of **1** and its derivatives starting from optically pure 2,2′-diamino-1,1′-binaphthyl via the optically active dibromide.[8] We now report a new, practical route to optically pure BINAP and its derivatives, which enables us to obtain various BINAP ligands in large quantities. The new procedure stems on the preparation of racemic dioxides of BINAP and its derivatives followed by optical resolution by use of readily available optically active organic acids.

Results and Discussion

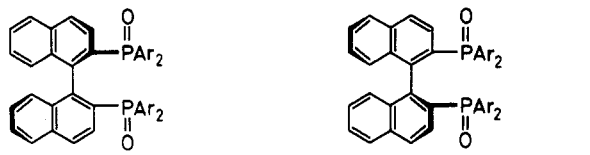
Synthesis of Optically Pure BINAPs. (±)-2,2′-Bis(diphenylphosphinyl)-1,1′-binaphthyl [(±)-**3**] (abbreviated to (±)-BINAPO) was prepared in 91% yield by condensation of the Grignard reagent derived from (±)-2,2′-dibromo-1,1′-binaphthyl (**2**) and diphenylphosphinyl chloride (eq 1). The optical resolution of (±)-BINAPO was performed in two ways. The first was a modification of the classic Meisenheimer method,[9] which was earlier utilized for resolution of phosphine oxides with phosphorus atom chirality. The original procedure used an equimolar amount of α-bromocamphorsulfonic acid to resolve monophosphine oxides. We found that the resolution of (±)-BINAPO was achievable by employing only 1 equiv of camphorsulfonic acid per two phosphine oxide functions. Thus, a mixture of equimolar amounts of (±)-**3** and (1*S*)-(+)-camphorsulfonic acid [(1*S*)-(+)-**6**] and excess *acetic acid* in ethyl acetate was heated at reflux until a clear solution was obtained. When this was cooled to 2–3 °C with stirring for a couple of hours, a crystalline complex consisting of (*R*)-(+)-**3**, (1*S*)-(+)-**6**, acetic acid, and ethyl acetate in 1:1:1:1 ratio was obtained. The molecular structure of this complex was determined by single-crystal *X*-ray analysis (vide infra). This complex was easily decomposed upon contact with water to give the optically pure phosphine oxide, (*R*)-(+)-**3**. The yield was 68% of theory.



2 (±)-3, Ar = C_6H_5 [(±)-BINAPO]
(±)-4, Ar = p-$CH_3C_6H_4$
(±)-5, Ar = p-t-$C_4H_9C_6H_4$ (1)



(1S)-(+)-6 (−)-7



(R)-(+)-3, Ar = C_6H_5 (S)-(−)-3, Ar = C_6H_5
(R)-(+)-4, Ar = p-$CH_3C_6H_4$ (S)-(−)-5, Ar = p-t-$C_4H_9C_6H_4$

The second and perhaps more convenient way for obtaining optically pure (+)- or (−)-**3** uses optically active (2*R*,3*R*)-(−)- or (2*S*,3*S*)-(+)-2,3-*O*-dibenzoyltartaric acid [(−)-**7** or (+)-**7**] as a resolving agent.[10] When a solution of (−)-**7** in ethyl acetate was added to a stirred boiling solution of (±)-**3** in chloroform, a white precipitate was formed in a few minutes. Recrystallization of the solid from the same solvent system afforded a diastereomerically pure complex of (*S*)-(−)-**3** and (−)-**7** in 79% yield. The free sample of (*S*)-(−)-**3** was obtained by treatment of the tartrate complex with aqueous base. The antipode, (*R*)-(+)-**3**, was recovered from the mother liquor of the

(1) Recent reviews: Markó, L.; Bakos, J. In "Aspects of Homogeneous Catalysis", Ugo, R., Ed.; Kluwer: Hingham, MA, 1981; Vol. 4, pp 145–202. Noyori, R.; Takaya, H. *J. Syn. Org. Chem. Jpn.* **1981**, *39*, 522. Kagan, H. B. In "Comprehensive Organometallic Chemistry"; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds. Pergamon Press: Oxford, 1982; Vol. 8, pp 463–498. Knowles, W. S.; Christopfel, W. C.; Koenig, K. E.; Hobbs, C. F. In "Catalytic Aspects of Metal Phosphine Complexes"; Alyea, E. C., Meek, D. W., Eds.; American Chemical Society: Washington, DC, 1982; Advances in Chemistry Series, No. 196, pp 325–388. Hayashi, T.; Kumada, M. *Acc. Chem. Res.* **1982**, *15*, 395. Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106. Brown, J. M.; Chaloner, P. A. "Homogeneous Catalysis with Metal Phosphine Complexes", Pignolet, L. H., Ed.; Plenum Press: New York, 1983; pp 137–165.

(2) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. Miyashita, A.; Takaya, H.; Souchi, T.; Noyori, R. *Tetrahedron*, **1984**, *40*, 1245.

(3) Toriumi, K.; Ito, T.; Takaya, H.; Souchi, T.; Noyori, R. *Acta Crystallogr. Sect. B: Struct. Sci.* **1982**, *B38*, 807.

(4) Noyori, R.; Takaya, H. *Chem. Scr.*, **1985**, *25*, 83.

(5) Inoue, S.; Osada, M.; Koyano, K.; Takaya, H.; Noyori, R. *Chem. Lett.* **1985**, 1007.

(6) Tani, K.; Yamagata, T.; Otsuka, S.; Akutagawa, S. Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R. *J. Chem. Soc., Chem. Commun.* **1982**, 600. Tani, K.; Yamagata T.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Am. Chem. Soc.* **1984**, *106*, 5208.

(7) Brown, K. J.; Berry, M. S.; Waterman, K. C.; Lingenfelter, D.; Murdoch, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 4717.

(8) In our experience, the procedure involving the usual Sandmeyer reaction of optically active 2,2′-diamino-1,1′-binaphthyl brought about considerable racemization of the products and was not very reproducible.[2,3] On the other hand, Murdoch and his coworkers successfully used the stable mercury halide salts of the diazonium ion followed by the thermal decomposition of the dry salt in the presence of excess KBr.[7] They also carried out the reaction of dilithiobinaphthyl with diphenylchlorophosphine in dimethyl ether at −130 °C.

(9) Meisenheimer, J.; Lichtenstadt, L. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 356. Meisenheimer, J.; Casper, J.; Höring, M.; Lauter, W.; Lichtenstadt, L.; Samuel, W. *Justus Liebigs Ann. Chem.* **1926**, *449*, 213.

(10) Brunner, H.; Pieronczyk, W.; Schönhammer, B.; Streng, K.; Bernal, I.; Korp, J. *Chem. Ber.* **1981**, *114*, 1137.

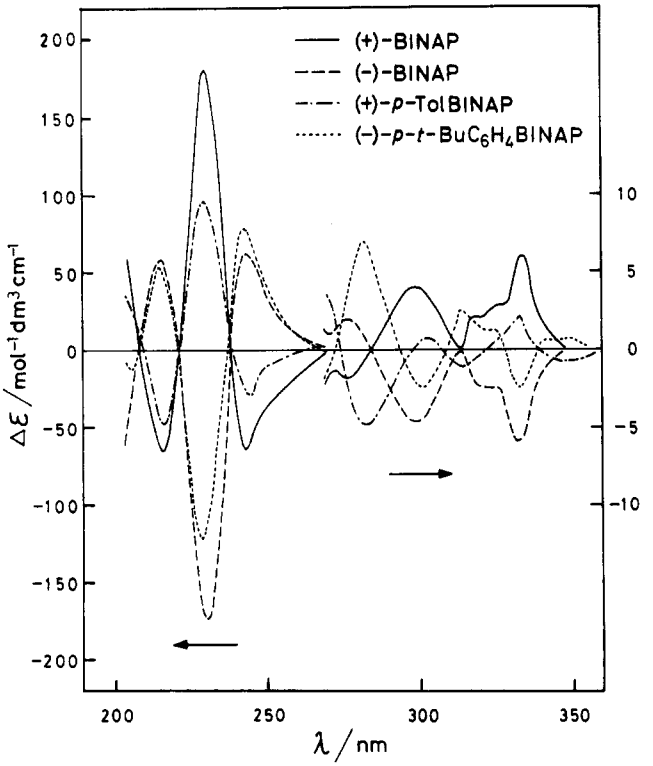
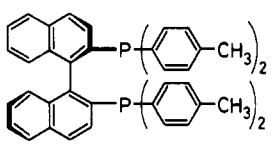


Figure 1. Circular dichroism spectra of (*R*)-(+)- and (*S*)-(-)-BINAP and their derivatives in ethanol.

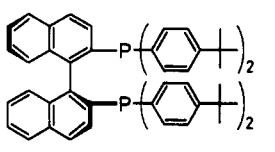
recrystallization by treatment with aqueous base. This crude product could be further purified by formation of the complex with (+)-**7**. The yield of optically pure (*R*)-(+)-**3** was 82% of theory. Thus, both (*S*)-(-) and (*R*)-(+) enantiomers were effectively obtained by choosing the handedness of the resolving agents.

Reduction of resolved BINAPO to BINAP proceeded without loss of optical purity in 95% yield by heating with a large excess of trichlorosilane and triethylamine in xylene.[11]

The present procedure can be extended to the synthesis of some BINAP analogues such as **8** and **9**. Optical resolutions of racemic diphosphine dioxides **4** and **5** were easily attained by forming diastereomeric complexes with (-)-**7** or (+)-**7** followed by recrystallization. The stereospecific conversion to optically pure diphosphines was performed by standard reduction with trichlorosilane and triethylamine. The absolute configurations of (+)-**8** and (-)-**9** were substantiated by comparing the CD spectra with those of (*R*)-(+)- and (*S*)-(-)-BINAP whose configurations have been determined by *X*-ray analysis.[3] Comparison of CD spectrum of (+)-**8** with that of (*R*)-(+)-BINAP (Figure 1) confirmed that this (+) enantiomer has the *R* configuration, while (-)-**9** exhibited a Cotton effect similar to that



(*R*)-(+)-**8**



(*S*)-(-)-**9**

of (*S*)-(-)-BINAP, showing that (-)-**9** has the *S* configuration. Thus, the present procedure is quite convenient and flexible for synthesis of original BINAP and its derivatives.

(11) Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012.

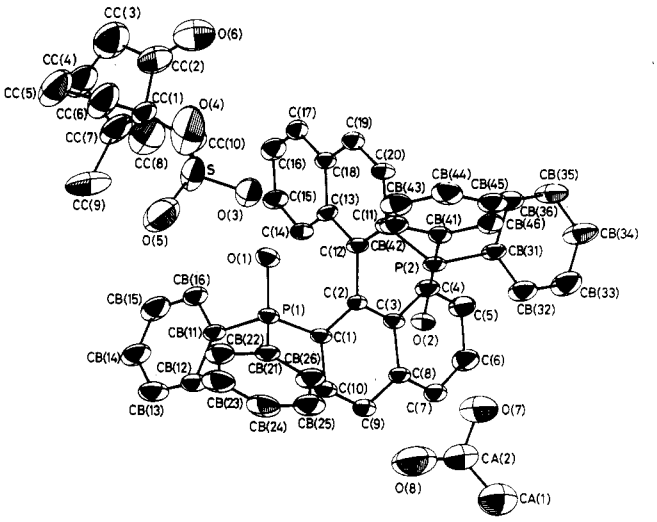


Figure 2. ORTEP drawing of the complex of (*S*)-(-)-BINAPO, (1*R*)-(-)-camphorsulfonic acid, and acetic acid, showing atomic labeling. Thermal ellipsoids are drawn at the 30% probability level. The crystal solvent ethyl acetate and all hydrogen atoms are omitted for simplicity.

Table I. Crystal Data for the Complex of (*S*)-(-)-3, (1*R*)-(-)-6, and Acetic Acid

formula	$C_{60}H_{60}O_{10}P_2S_1$
fw	1035.14
cryst system	triclinic
a, Å	10.340(1)
b, Å	15.567(1)
c, Å	9.212(1)
α, deg	76.79(1)
β, deg	107.00(1)
γ, deg	101.68(1)
V, Å^3	1365.7(3)
Z	1
D_{calcd}, g/cm^3	1.261
space group	*P*1
crystal size, mm	0.14 × 0.28 × 0.42
μ(Cu Kα), cm^{-1}	13.11
diffractometer	Rigaku AFC-5
scan type	θ–2θ
scan speed, deg/min	3
scan range, deg	1.3 + 0.3 tan θ
data collected	$\pm h,\pm k,\pm l$
$2\theta_{max}$, deg	120
no. of reflctns ($\|F_o\| > 3\sigma(F_o)$)	7842
no. of variables	833
R, %	5.96
R_w, %	7.08

X-ray Structure of the Complex of (*S*)-(-)-BINAPO, (1*R*)-(-)-Camphorsulfonic Acid, and Acetic Acid. In order to obtain information on the molecular structure of the complex of (*S*)-(-)-**3**, (1*R*)-(-)-**6**, and acetic acid, an *X*-ray analysis was done on the colorless needles obtained by recrystallization from a hot mixture of ethyl acetate and acetic acid. The crystals remained intact in the closed vessel saturated with ethyl acetate vapor, but became opaque and brittle in the open air. A suitable crystal was sealed in a capillary in an argon atmosphere saturated with ethyl acetate vapor. Crystal data are listed in Table I. An ORTEP drawing of the complex with labeling scheme is shown in Figure 2. Figure 3 shows a stereoview of the crystal structure of the complex, which also contains an ethyl acetate molecule as crystal solvent. Selected bond lengths and angles are compiled in Table II. The angle between the least-squares planes of two naphthyl rings is 90.30 (7)°. One of the oxygen atoms of the two P=O groups interacts with camphorsulfonic acid through hydrogen bonding (O(1)–O(3) = 2.414 (5) Å)[12] and another

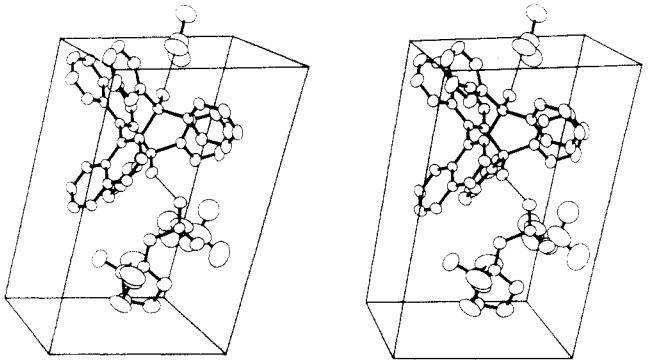


Figure 3. ORTEP stereoview of the unit cell of the complex of (*S*)-(−)-BINAPO, (1*R*)-(−)-camphorsulfonic acid, and acetic acid, illustrating the intermolecular hydrogen bonds between phosphine oxides and acid functions. Hydrogen bonds are shown by solid lines. All hydrogens are removed for clarity.

Table II. Selected Interatomic Distances (Å) and Angles (degree) with ESD's

	a. (−)-BINAPO		
P1–O1	1.506 (3)	P1–C1	1.785 (4)
P1–CB11	1.798 (5)	P1–CB21	1.787 (4)
P2–O2	1.483 (3)	P2–C11	1.812 (4)
P2–CB31	1.801 (4)	P2–CB41	1.797 (4)
O1–P1–C1	111.9 (2)	O1–P1–CB11	109.8 (2)
O1–P1–CB21	112.5 (2)	C1–P1–CB11	106.1 (2)
C1–P1–CB21	108.6 (2)	CB11–P1–CB21	107.7 (2)
O2–P2–C11	114.9 (2)	O2–P2–CB31	112.2 (2)
O2–P2–CB41	111.5 (2)	C11–P2–CB31	104.6 (2)
C11–P2–CB41	105.9 (2)	CB31–P2–CB41	107.1 (2)
	b. (−)-Camphorsulfonic Acid		
S–O3	1.492 (5)	S–O4	1.437 (11)
S–O5	1.334 (8)	S–CC10	1.737 (6)
O3–S–O4	106.6 (5)	O3–S–O5	111.2 (4)
O3–S–CC10	103.6 (3)	O4–S–O5	118.6 (6)
O4–S–CC10	106.0 (5)	O5–S–CC10	109.8 (4)
	c. Acetic Acid		
O7–CA2	1.281 (11)	O8–CA2	1.172 (12)
O7–CA2–O8	119.1 (9)	O7–CA2–CA1	115.6 (8)
O8–CA2–CA1	125.1 (9)		
	d. Others		
O1–O3	2.414 (5)	O2–O7	2.609 (6)
P1–O1–O3	141.3 (2)	P2–O2–O7	135.6 (2)
O1–O3–S	113.0 (3)	O2–O7–CA2	124.0 (5)

oxygen atom has a hydrogen bond interaction with acetic acid (O(2)–O(7) = 2.609 (6) Å),[12] minimizing the quantity of the chiral resolving agent. Thus, enantiomer separation has been successfully attained by preferential crystallization of one of the diastereomeric inclusion compounds formed from the host substance, (−)-**3**, and the optically active guest, (1*R*)-(−)-**6**.[13] The absolute configuration of (−)-BINAPO was elucidated as *S* by being correlated with the known configuration of (1*R*)-(−)-**6**.

Experimental Section

Apparatus. Proton nuclear magnetic resonance (^{1}H NMR) spectra were determined with a Varian EM390 (90 MHz) or a JEOL JNM-GX400 (400 MHz) spectrometer using tetramethylsilane as the internal standard. ^{31}P NMR spectra were measured on a JEOL JNM-GX400 (161 MHz) and chemical shifts were reported in ppm relative to 85% phosphoric acid as the external standard. Other spectra were recorded with the use of the following instruments: IR, Hitachi 295; UV, Shimadzu UV-260; optical rotation, JASCO DIP-4; CD, JASCO J-40C; low-resolution mass (LRMS) and high-resolution mass spectra (HRMS), JEOL JMS-D300. Gas chromatographic (GLC) analyses were conducted on a Hitachi 263-30 equipped with a flame-ionization detector and a capillary column (OV-101, 5 m). The analyses were done at an injection temperature of 280 °C and by raising the column temperature from 200 to 280 °C at a rate of 10 °C/min. All melting points were uncorrected. Elemental analyses were performed either at Shonan Analytical Center Co. or at Wako Pure Chemical Industry, Ltd.

Chemicals. 2,2′-Dibromo-1,1′-binaphthyl (**2**) was prepared according to the literature method.[2,3] Diphenylphosphinyl chloride was prepared either by oxidation of diphenylphosphinous chloride with dimethyl sulfoxide[14] or by the treatment of diphenylphosphinic acid with phosphorus pentachloride.[15] Di-*p*-tolylphosphinyl chloride was also synthesized according to the reported procedure.[16] Bis(*p*-*tert*-butylphenyl)phosphinyl chloride was prepared by the acid hydrolysis of Bis(*p*-*tert*-butylphenyl)-phosphine *N*,*N*-diethylamide (mp 286 °C) followed by the treatment of resulting bis(*p*-*tert*-butylphenyl)phosphinic acid with thionyl chloride.[17] Commercial (1*S*)-(+)- and (1*R*)-(−)-camphorsulfonic acid, (2*R*,3*R*)-(−)- and (2*S*,3*S*)-(+)-2,3-di-*O*-benzoyltartaric acid monohydrate, and trichlorosilane were used as obtained. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl or 70% sodium bis(2-methoxyethoxy)aluminium hydride in toluene under argon. Triethylamine was distilled over BaO. Other solvents and reagents were guaranteed grade and distilled before use.

Synthesis of 2,2′-Bis(diphenylphosphinyl)-1,1′-binaphthyl [(±)-3] [(±)-BINAPO]. In a 1-L four-necked, round-bottomed flask equipped with a mechanical stirrer, a reflux condenser, a thermometer, and an addition funnel were placed magnesium chips (2.62 g, 0.108 g-atom) and the flask was flushed with nitrogen. To this were added iodine (50 mg), THF (40 mL), and 1,2-dibromoethane (0.51 mL). The mixture was stirred at room temperature until the color of iodine faded, and to this was added dropwise a solution of 2,2′-dibromo-1,1′-binaphthyl (20.0 g, mp 187–188 °C, 95.5% purity by GLC analysis, 46.4 mmol) in toluene (360 mL) via the addition funnel over a period of 4 h at 50–75 °C. The reaction mixture was further stirred at 75 °C for 2 h and was then cooled to 0 °C. To this was added dropwise a solution of diphenylphosphinyl chloride (23.2 g, 98.0 mmol) in toluene (23 mL) during 30 min, holding the temperature at 0–5 °C. After the addition was completed, the mixture was further stirred at 60 °C for 3 h and then cooled to ambient temperature. Water (60 mL) was added to this and the mixture was stirred at 60 °C for 10 min. The organic layer was separated, washed with water, and concentrated to a volume of 60 mL under reduced pressure. The residue was left overnight at ambient temperature, and crystalline material was collected on a glass funnel. The product was stirred for 10 min with a mixture of heptane (45 mL) and toluene (5 mL), collected on a glass funnel, and dried at 70 °C (1 mm) for 24 h to give 27.5 g (91%) of (±)-**3** as an essentially pure compound, mp 295–298 °C. Concentration of the mother liquor gave 4.0 g of brown crystals, mp 150 °C. GLC analysis of this product indicated contamination of some (±)-**3**, but its isolation was not carried out. The analytical sample of (±)-**3** was obtained by recrystallization from a mixture of heptane and toluene followed by drying at 80 °C (1 mm) overnight, mp 304–306 °C: ^{1}H NMR ($CDCl_3$) δ 6.80 (d, 4 H, J = 3.7 Hz), 7.15–7.30 (m, 8 H), 7.32–7.48 (m, 12 H), 7.65–7.73 (m, 4 H), 7.78–7.88 (m, 4 H); ^{31}P NMR ($CDCl_3$) δ 30.7 ppm; IR (KBr) ν 3045 (m), 1587 (w), 1551 (w), 1503 (w), 1484 (w), 1434 (s), 1307 (m), 1258 (w), 1196 (s), 1112 (s), 1161 (w), 1022 (w), 996 (w), 872 (m), 849 (w), 815 (m), 743 (s), 721 (s), 699 (s), 646 (m), 631 (w), 572 (m), 539 (s), 515 (s), 481 (m), 433 (m) cm^{-1}; LRMS (30 eV), m/z (% intensity) 655 (M^+

(12) Kuleshova, L. N.; Zorkii, P. M. *Acta Crystallogr. Sect. B: Struct. Sci.* **1981**, *B37*, 1363.

(13) Arad-Yellin, R.; Green, B. S.; Knossow, M.; Tsoucaris, G. "Inclusion Compounds"; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Academic Press: London, 1984; Vol. 3, pp 263–292.

(14) Amonoo-Neizer, E. H.; Ray, S. K.; Shaw, R. A.; Smith, B. C. *J. Chem. Soc.* **1965**, 4296.

(15) Higgins, Wm. A.; Vogel, P. W.; Craig, W. G. *J. Am. Chem. Soc.* **1955**, *77*, 1864.

(16) Michaelis, A. *Justus Liebigs Ann. Chem.* **1901**, *315*, 43. Mallion, K. B.; Mann, F. G. *J. Chem. Soc.* **1964**, 5716. Kosolapoff, G. M. *J. Am. Chem. Soc.* **1949**, *71*, 369. Kosolapoff, G. M.; Powell, J. S. *J. Chem. Soc.* **1950**, 3535.

(17) Kosolapoff, G. M. *J. Am. Chem. Soc.* **1949**, *71*, 369. Issleib, K.; Brack, A. *Z. Anorg. Allg. Chem.* **1954**, *277*, 258.

+ 1, 0.2), 654 (M^+, 0.3), 653 ($M^+ - 1$, 0.2), 577 ($M^+ - C_6H_5$, 1.1), 455 (6.1), 454 (36), 453 ($M^+ - (C_6H_5)_2PO$, 100), 201 ($(C_6H_5)_2PO$, 2.1). Anal. Calcd for $C_{44}H_{32}O_2P_2$: C, 80.72; H, 4.93; P, 9.46. Found: C, 80.88; H, 4.68; P, 9.03.

Optical Resolution of (±)-BINAPO [(±)-3] with (1*S*)-(+)-6. In a 1-L three-necked, round-bottomed flask equipped with a reflux condenser, a dropping funnel, a thermometer, and a magnetic stirring bar were added (±)-**3**, (65.4 g, 0.100 mol), the monohydrate of (1*S*)-(+)-**6** (25.0 g, 0.100 mol), and ethyl acetate (270 mL), and the mixture was heated at reflux. To this was added dropwise acetic acid (90 mL), and heating was continued until a clear solution was obtained. The mixture was gradually cooled to 2–3 °C with stirring over a period of 2 h, and stirring was continued for an additional 30 min. The solid material was collected on a glass funnel and washed with cold ethyl acetate (100 mL) to give 35.3 g (68% based on initially used (*R*)-**3**) of a 1:1:1 complex of (*R*)-(+)-**3**, (1*S*)-(+)-**6**, and acetic acid. This complex did not exhibit any sharp melting point, $[\alpha]^{24}_D$ +99.4° (*c* 1.5, methanol). Combustion analysis and NMR spectrum of this complex revealed that it contains an equimolar amount of ethyl acetate as a crystal solvent. Anal. Calcd for $C_{60}H_{60}O_{10}P_2S$: C, 69.6; H, 5.84; P, 5.98; S, 3.10. Found: C, 69.6; H, 5.9; P, 6.1; S, 3.1. ^1H NMR ($CDCl_3$): signals due to camphorsulfonic acid, δ 0.80, 1.07 (two s, $2CH_3$), 1.24–1.33 (m, H_{5n}, $J_{5n,6x}$ = 3.8 Hz, $J_{5n,6n}$ = 9.2 Hz), 1.50–1.58 (m, H_{6n}, $J_{6x,6n}$ = 11.3 Hz), 1.85 (A part of ABq, H_{3n}, $J_{3n,3x}$ = 18.4 Hz), 1.90–2.00 (m, H_{5x}, $J_{5x,6x}$ = 12.0 Hz, $J_{3x,5x}$ = 3.0 Hz), 2.00 (broad s, H_4), 2.32 (B part of ABq, H_{3x}, $J_{3x,4}$ = 3.0 Hz), 2.55 (dt, H_{6x}), 2.81, 3.32 (ABq, C_{10} methylene), 10.51 (broad s, hydroxylic protons); absorptions due to acetic acid and ethyl acetate, 1.26 (t, *J* = 7.3 Hz, OCH_2CH_3), 1.98 (s, CH_3COOH), 2.04 (s, $CH_3COOC_2H_5$), 4.12 (q, OCH_2CH_3); aromatic protons, 6.70 (d, 2 H, *J* = 8.4 Hz), 6.88 (t, 2 H, *J* = 8.4 Hz), 7.12–7.54 (m, 20 H), 7.70–7.94 (m, 8 H). IR (KBr): ν 3425 (s), 3065 (m), 2965 (m), 1745 (s), 1643 (m), 1590 (w), 1434 (m), 1372 (m), 1303 (w), 1260 (w), 1238 (w), 1173 (s), 1113 (s), 1043 (m), 862 (m), 814 (m), 747 (m), 722 (m), 697 (s), 647 (w), 612 (w), 574 (m), 538 (s), 512 (s), 488 (w), 433 (w) cm^{-1}. This complex was suspended in toluene (390 mL) and heated at 80 °C for a short time. Then water (30 mL) was added to this mixture to decompose the complex. The organic layer was separated and washed with two 30-mL portions of water. The toluene layer was concentrated to the volume of 50 mL and to the remaining mixture was added hexane (50 mL). The crystals were separated by filtration and dried in vacuo to give (*R*)-**3** (22.2 g, 68% based on (*R*)-**3** used), mp 262–263 °C, $[\alpha]^{24}_D$ + 399° (*c* 0.5, benzene): UV (ethanol) λ_{max} 229 (ε 100 000), 273 (13 000), 288 (12 000), 298 (sh, 11 000), 316 (sh, 3400), 332 (3600) nm.

The mother liquor obtained after the separation of the complex of (*R*)-**3** and (1*S*)-**6** was concentrated in vacuo and to the residue was added toluene (1.9 L). The mixture was heated at 80 °C and extracted 3 times with 100 mL of water. The organic layer was concentrated to 150 mL and to this was added hexane (150 mL). The mixture was allowed to stand at room temperature for 2 h. The solid precipitated was collected on a glass funnel to give crude (*S*)-**3** (40.6 g), $[\alpha]^{24}_D$ −211.6° (*c* 0.5, benzene). This product was calculated to be a mixture of 76.5% (*S*)-**3** and 23.5% (*R*)-**3**. Further experiments for obtaining optically pure (*S*)-**3** from this sample were not carried out. The combined water layer was concentrated to give 24.0 g (96% recovery) of (1*S*)-(+)-**6** monohydrate.

When (1*R*)-(−)-**6** was used as the resolving agent in place of (1*S*)-(+)-**6**, we obtained optically pure (*S*)-(−)-**3** in a comparable yield as has been detailed above for (1*R*)-(−)-**6**.

Optical Resolution of (±)-BINAPO [(±)-3] with (−)-7 or (+)-7. To a boiling solution of (±)-**3** (5.00 g, 7.64 mmol) in chloroform (350 mL) was added rapidly a warm solution of monohydrate of (−)-**7** (2.88 g, 7.65 mmol) in ethyl acetate (230 mL). The mixture was refluxed with stirring for a further 5 min, and then allowed to stand at ambient temperature overnight. The white precipitates were separated by a glass funnel, and the filtrate was stored for the recovery of (*R*)-(+)-**3**. The solid product was dried at room temperature (0.05 mm) for 30 min to give 3.32 g (86% based on (*S*)-(−)-**3** used) of a 1:1 complex of (*S*)-**3** and (−)-**7**, mp 232–243 °C (dec), $[\alpha]^{24}_D$ −171.8° (*c* 0.445, ethanol). This complex was dissolved as much as possible in boiling chloroform (210 mL) and then to this was added gradually ethyl acetate (280 mL). The mixture was heated at reflux for 10 min. The crystals separated after being allowed to stand at room temperature for 48 h were collected by filtration and dried at room temperature (0.05 mm) to afford 3.04 g (79% based on (*S*)-**3** initially used) of the (*S*)-**3**-(−)-**7** complex, mp 236–237 °C (dec), $[\alpha]^{24}_D$, −165.4° (*c* 0.412, ethanol). The above result shows that no substantial change in optical rotation occurred by recrystallization, which indicates that the first crop of the complex was pure enough. The analytical sample was obtained by further recrystallization from a mixture of chloroform and ethyl acetate, mp 240–241 °C dec. ^1H NMR ($CDCl_3$): δ 5.93 (s, 2C*H*OCO), 6.74–6.84 (m, 4 H), 7.09–7.16 (m, 4 H), 7.22–7.47 (m, 18 H), 7.55–7.68 (m, 8 H), 7.72–7.84 (m, 4 H), 8.08 (d, 4 H, *J* = 7.02 Hz). Absorptions due to hydroxylic protons could not be observed. IR (KBr): ν 3440 (m), 3055 (w), 2940 (w), 1738 (s), 1723 (m), 1642 (w), 1451 (w), 1435 (m), 1328 (w), 1314 (w), 1255, (m), 1236 (m), 1171 (s), 1152 (w), 1105 (m), 1067 (w), 1022 (w), 867 (w), 810 (m), 750 (m), 740 (m), 719 (s), 701 (m), 651 (w), 572 (m), 536 (m), 513 (m), 489 (w), 438 (w) cm^{-1}. Anal. Calcd for $C_{62}H_{46}O_{10}P_2$: C, 73.51; H, 4.58. Found: C, 73.54; H, 4.65.

The above complex (2.80 g, 2.76 mmol) was treated with 0.75 N NaOH (70 mL) and the mixture was extracted with two 75-mL portions of chloroform. The combined organic layer was washed with 0.75 N NaOH (30 mL), water, and dried over Na_2SO_4. Evaporation of the solvent furnished white solid (2.05 g) which was washed with ethyl acetate (20 mL), and dried at 80 °C (0.05 mm) overnight to give 1.71 g (95% based on the complex used) of (*S*)-**3**, mp 258–259 °C $[\alpha]^{25}_D$ −389° (*c* 0.511, benzene).

The mother liquor which contained the (*R*)-**3**-(−)-**7** complex was concentrated to dryness to give 4.10 g of solid material, mp 226–227 °C dec. This was treated with 60 mL of 1 N NaOH and extracted with two 75-mL portions of chloroform. The combined extract was washed with 1 N NaOH (20 mL), water (100 mL), and dried over Na_2SO_4. Evaporation of the solvent gave crude (*R*)-**3** (2.90 g), mp 256–258 °C, $[\alpha]^{20}_D$ +278° (*c* 0.512, benzene). This recovered (*R*)-**3** (2.90 g, 4.43 mmol) was dissolved in refluxing chloroform (170 mL) and to this was added with stirring a solution of (*R*)-**7** monohydrate (1.67 g, 4.44 mmol) in ethyl acetate (140 mL). The mixture was stirred at reflux temperature for 5 min and then allowed to stand at room temperature overnight. The white precipitates were collected on a glass funnel, washed with two 10-mL portions of ethyl acetate, and dried at room temperature (0.05 mm) for 1 h to give 3.25 g (84% yield based on the initially used (*R*)-**3**) of the (*R*)-**3**-(+)-**7** complex, mp 235–236 °C dec, $[\alpha]^{20}_D$ +170° (*c* 0.384, ethanol). This complex (3.25 g, 3.21 mmol) was treated with 0.75 N NaOH (110 mL) and extracted twice with each 75 mL of chloroform. The combined chloroform layer was washed with 0.75 N NaOH (30 mL), water (100 mL), and dried over Na_2SO_4. Evaporation of the solvent afforded 2.07 g (82% yield based on (*R*)-**3** used) of (*R*)-**3**, mp 258–259 °C, $[\alpha]^{20}_D$ +391° (*c* 0.447, benzene).

Reduction of (*S*)-(−)-BINAPO [(*S*)-3] to (*S*)-(−)-BINAP [(*S*)-(−)-1]. This experiment is illustrative for the reduction of (*S*)- or (*R*)-**3** into (*S*)- or (*R*)-**1**, respectively. In a 1-L three-necked flask equipped with a thermometer and a reflux condenser which is connected to an argon inlet tube and a bubbler through a three-way stopcock, was placed (*S*)-**3** (50.0 g, 76.4 mmol). The flask was flushed with argon and to this was added dry xylene (500 mL), triethylamine (32.4 g, 320 mmol), and trichlorosilane (41.4 g, 306 mmol). The mixture was stirred and heated at 100 °C for 1 h, at 120 °C for 1 h, and finally at refluxing temperature for 5 h. After cooling to room temperature, 30% aq NaOH (135 mL) was added carefully to the mixture. It was then stirred at 60 °C until organic and aqueous layers became clear. The organic layer was separated and concentrated under reduced pressure. To the residue was added methanol (200 mL) and the precipitates were collected on a glass funnel to give 47.3 g (95%) of (*S*)-**1**, mp 241–242 °C, $[\alpha]^{24}_D$ −228° (*c* 0.679, benzene). GLC analysis indicated that the product had a purity of 97.1%. UV (ethanol): λ_{max} 222 (ε 100 000), 235 (sh, 91 000) nm.

Synthesis of (±)-2,2'-Bis(di-*p*-tolylphosphinyl)-1,1'-binaphthyl [(±)-4]. In a 2-L three-necked, round-bottomed flask fitted with a reflux condenser, a dropping funnel, and a mechanical stirrer were placed magnesium chips (6.90 g, 0.284 g-atom), THF (90 mL), and toluene (210 mL), and to this were added 1,2-dibromoethane (0.5 mL) and a catalytic amount of iodine. The

mixture was heated at reflux with stirring for several minutes, and then to this was added dropwise a solution of the dibromide **2** (55.2 g, 90% purity, 0.121 mol) in toluene (400 mL) containing 0.5 mL of 1,2-dibromoethane over a period of 5 h, holding the temperature of the mixture at 70–80 °C. The Grignard reagent formed deposited during the addition of the dibromide. After the addition of **2** was completed, the mixture was cooled to 40–45 °C. To this was added a solution of di-*p*-tolylphophinyl chloride (66.9 g, 0.253 mol) in toluene (100 mL) during 1 h and stirring was continued for another hour in the same temperature range. The solvent was removed at 60 °C under reduced pressure. To the residue was added water (250 mL) and the mixture was extracted with 1,2-dichloroethane (300 mL). The organic layer was separated and the solvent was evaporated to give 121 g of solid product. Recrystallization from a mixture of 1,2-dichloroethane (400 mL) and toluene (200 mL) gave 58.5 g (60%) of (±)-**4**. This compound partially melted at 178–185 °C, but at a higher temperature solidified and then melted at 311–316 °C. Upon concentration of the mother liquor, the second crop (18.1 g, 19%) was obtained, mp 310–315 °C. TLC analysis (silica gel, R_f 0.30, 1:1 hexane–acetone) exhibited only one spot. ^{1}H NMR ($CDCl_3$) indicated that the product is a 1:1 complex of (±)-**4** and toluene: δ 2.28 (s, CH_3), 2.32 (s, CH_3), 2.36 (s, CH_3), and 6.85–7.92 (m, 33 H, aromatic protons). The crystals lost toluene when heated at 80 °C (1 mm) overnight, mp 311–316 °C. IR (KBr): ν 3040 (w), 2915 (w), 2850 (w), 1596 (m), 1551 (w), 1501 (m), 1448 (m), 1397 (m), 1307 (m), 1257 (w), 1211 (m), 1200 (s), 1182 (m), 1111 (s), 1093 (m), 1019 (m), 871 (m), 847 (w), 808 (s), 772 (w), 743 (m), 711 (m), 690 (m), 676 (w), 649 (s), 636 (w), 623 (w), 571 (m), 524 (s), 511 (s), 484 (m), 460 (m), 447 (m) cm^{-1}. LRMS (30 eV): *m/z* (% intensity) 710 (M^+, 0.1), 709 (0.2), 619 ($M^+ - C_7H_7$, 1.0), 483 (7.7), 482 (39), 481 ($M^+ - (CH_3C_6H_4)_2PO$, 1000), 480 (1.9), 479 (2.7), 230 (1.4), 229 ($(CH_3C_6H_4)_2PO$, 6.1).

Optical Resolution of (±)-4 with (–)-7. In a 1-L flask were placed the 1:1 complex of (±)-**4** and toluene (41.2 g, 51.3 mmol) and (–)-**7** monohydrate (19.3 g, 51.3 mmol) and to this was added chloroform (190 mL). The mixture was heated at reflux until a homogeneous solution was obtained. Ethyl acetate (500 mL) was added dropwise at the refluxing temperature, and the mixture was allowed to stand at room temperature overnight to give 29.9 g of a 1:1:1 complex of (*R*)-**4**, (–)-**7**, and ethyl acetate, mp 163–166 °C, $[\alpha]^{24}_D$ +22.9° (*c* 0.654, chloroform). Recrystallization of the product from the same solvent system gave 21.6 g (72% yield based on the initially used (*R*)-**4**) of the complex, mp 164–168 °C, $[\alpha]^{24}_D$ +25.3° (*c* 0.986, chloroform). No essential changes in optical rotation and melting point were observed after further recrystallization. ^{1}H NMR ($CDCl_3$): signals due to (–)-**7**, δ 5.94 (s, 2CHOCO), 7.32–7.38 (m, 4 H_{meta}), 7.46–7.54 (m, 2 H_{para}), 8.03 (d with fine splitting, 4 H_{ortho}, J = 7.8 Hz); signals due to (*R*)-**4**, 2.21 (s, 2 CH_3), 2.27 (s, 2 CH_3), 6.75–6.83 (m, 6 H), 6.86–6.91 (m, 2 H), 6.97–7.06 (m, 8 H), 7.32–7.38 (m, 2 H), 7.44–7.53 (m, 6 H), 7.70–7.79 (m, 4 H); signals due to ethyl acetate, 1.26 (t, J = 7.3 Hz, CH_2CH_3), 2.05 (s, CH_3CO), 4.12 (q, CH_2CH_3). The above complex lost ethyl acetate when it was kept at 80 °C (0.05 mm) overnight. ^{1}H NMR ($CDCl_3$): signals due to (–)-**7**, δ 6.12 (s, 2 CHOCO), 7.34–7.41 (t-like, 4 H_{meta}, J = 6.4 Hz), 7.47–7.56 (m, 2 H_{para}), 8.07 (d with fine splitting, 4 H_{ortho}, J = 7.9 Hz) signals due to (*R*)-**4**, 2.17 (s, 2 CH_3), 2.37 (s, 2 CH_3), 6.65–6.74 (m, 6 H), 6.91 (t, 2 H, J = 7.0 Hz), 6.94–7.00 (dd, 4 H, J = 8.2 and 12.2 Hz), 7.18–7.30 (m, 4 H), 7.34–7.41 (t-like, 2 H), 7.47–7.56 (m, 2 H), 7.58–7.67 (dd, 4 H, J = 8.2 and 12.2 Hz), 7.73 (d, 2 H, J = 8.2 Hz), 7.85 (d with fine splitting, 2 H, J = 8.8 Hz). Ir (KBr): ν 3430 (m), 3051 (w), 2920 (w), 2854 (w), 1731 (s), 1600 (m), 1503 (w), 1451 (m), 1398 (w), 1339 (w), 1313 (w), 1242 (m), 1166 (m), 1110 (s), 1092 (m), 1067 (m), 1023 (w), 869 (w), 845 (w), 804 (m), 741 (m), 709 (s), 588 (w), 650 (m), 567 (w), 522 (s), 460 (m) cm^{-1}. Anal. Calcd for $C_{66}H_{54}O_{10}P_2$: C, 74.15; H, 5.09; P, 5.79. Found: C, 73.74; H, 4.97; P, 5.81. The complex obtained above was dissolved in chloroform and treated with an excess of 1 N NaOH solution. The organic layer was dried over Na_2SO_4, concentrated, and the residue was dried overnight at 80 °C (1 mm) to give 11.3 g (15.9 mmol, 62% yield based on (*R*)-**4** used) of free (*R*)-**4**, mp 305–312 °C, $[\alpha]^{24}_D$ +135.2° (*c* 1.306, chloroform). UV (ethanol): λ_{max} 232 (ε 110 000), 275 (12 000), 287 (12 000), 299 (sh, 10 000), 316 (sh, 3500), 332 (3400) nm. Anal. Calcd for $C_{48}H_{40}O_2P_2$: C, 81.11; H, 5.67; P, 8.72. Found: C, 80.51; H, 5.80; P, 8.38. ^{1}H NMR ($CDCl_3$): δ 2.26 (s, 2 CH_3), 2.32 (s, 2 CH_3), 6.88 (d, 4 H, J = 4.3 Hz), 6.93–6.98 (m, 4 H), 7.01–7.07 (m, 4 H), 7.25–7.53 (m, 12 H), 7.77–7.83 (m, 4 H) (aromatic protons). ^{31}P NMR ($CDCl_3$): 29.8 ppm.

Similarly, the (*S*)-**4**–(+)-**7**–ethyl acetate complex (18.6 g, 72% based on (–)-**4**) was obtained from the 1:1 complex of (±)-**4** and toluene (35.6 g, 44.3 mmol) and (+)-**7** monohydrate (16.7 g, 44.4 mmol), $[\alpha]^{24}_D$ –23.1° (*c* 0.849, chloroform). Anal. Calcd for $C_{66}H_{54}O_{10}P_2$: C, 74.15; H, 5.09; P, 5.79. Found: C, 73.64; H, 5.19; P, 5.82. The complex obtained above afforded 10.7 g (68% based on (*S*)-**4** used) of free (*S*)-**4** upon treatment with base as described above, $[\alpha]^{24}_D$ –136.3° (*c* 1.039, chloroform). Anal. Calcd for $C_{48}H_{40}O_2P_2$: C, 81.11; H, 5.67; P, 8.72. Found: C, 80.73; H, 5.70; P, 8.41.

Reduction of (*R*)-(+)-4 to (*R*)-*p*-TolBINAP [(*R*)-(+)-8]. A 1-L three-necked, round-bottomed flask was fitted with a reflux condenser, a thermometer, and a magnetic stirring bar. The top of the condenser was equipped with a three-way stopcock which was connected with a gas babbler and an argon inlet tube. In the flask was placed a mixture of the phosphine oxide (*R*)-**4** (11.3 g, 15.9 mmol), triethylamine (17.7 g, 175 mmol), and trichlorosilane (21.5 g, 159 mmol) in xylene (200 mL). This mixture was kept with stirring successively at 80 °C for 0.5 h, 110 °C for 0.5 h, 120 °C for 0.5 h, and finally 130 °C for 5 h. After cooling the reaction mixture to room temperature, 30% aq NaOH (70 mL) was added, and the mixture was stirred at 60 °C for 10 min. The organic layer was separated and dried over Na_2SO_4 and the solvent was removed in vacuo. The residue was recrystallized from methanol to give optically pure (*R*)-(+)-TolBINAP [(*R*)-**8**] (10.2 g, 95%), mp 257–258 °C, $[\alpha]^{24}_D$ +174.0° (*c* 0.886, benzene): ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 2 CH_3), 2.25 (s, 2 CH_3), 6.83–7.00 (m, 20 H), 7.33–7.40 (m, 2 H), 7.42–7.48 (m, 2 H), 7.81–7.89 (four lines, 4 H); ^{31}P NMR ($CDCl_3$) –16.1 ppm; IR (KBr) ν 3010 (w), 2910 (w), 2855 (w), 1594 (w), 1549 (w), 1495 (m), 1443 (w), 1394 (w), 1308 (m), 1257 (w), 1211 (w), 1182 (m), 1109 (w), 1085 (m), 1015 (m), 960 (w), 943 (w), 866 (w), 839 (w), 802 (s), 771 (m), 745 (m), 710 (w), 692 (m), 643 (w), 628 (w), 614 (w), 573 (w), 511 (s), 494 (m), 468 (m), 432 (w), 420 (w), 405 (w), 386 (w) cm^{-1}; LRMS (30 eV), *m/z* (% intensity) 678 (M^+, 0.05), 677 (0.6), 482 (18), 481 (26), 466 (100), 465 ($M^+ - (CH_3C_6H_4)_2P$, 90), 339 (17), 282 (6), 281 (12), 213 ($(CH_3C_6H_4)_2P$, 9), 211 (7); UV (ethanol) λ_{max} 223 (ε 95 000), 236 (sh, 79 000) nm. Anal. Calcd for $C_{48}H_{40}P_2$: C, 84.93; H, 5.94; P, 9.13. Found: C, 84.86; H, 5.71; P, 8.84.

Similarly, (*S*)-**4** (10.7 g, 15.1 mmol) was reduced with trichlorosilane (20.4 g, 151 mmol) and triethylamine (16.7 g, 165 mmol) to give 9.7 g (95%) of (*S*)-**8**, mp 257–258 °C, $[\alpha]^{24}_D$ –169.5° (*c* 1.052, benzene). ^{1}H NMR spectrum of (*S*)-**8** was superimposable with that of (*R*)-**8**. Anal. Calcd for $C_{48}H_{40}P_2$: C, 84.93; H, 5.94; P, 9.13. Found: C, 84.74; H, 6.08; P, 8.91.

Synthesis of (±)-2,2′-Bis[bis(*p*-*tert*-butylphenyl)phosphinyl]-1,1′-binaphthyl [(±)-5]. The Grignard compound was prepared as described for the preparation of (±)-BINAPO, by the addition of the dibromide **2** (11.4 g, 90% purity, 24.9 mmol) in toluene (60 mL) to a stirred mixture of magnesium chips (1.50 g, 0.062 g-atom) and THF (30 mL). To this was added dropwise a solution of di(*p*-*tert*-butylphenyl)phosphinyl chloride (17.5 g, 50.2 mmol) in toluene (50 mL) at 0–5 °C. The reaction mixture was kept at 60 °C with stirring for 3 h. After workup as described for (±)-BINAPO, there obtained 25 g of crude (±)-**5** which was purified by recrystallization from a mixture of toluene and hexane to give 14 g (64%) of essentially pure (±)-**5**, mp 321–322 °C: LRMS (70 eV), *m/z* (% intensity) 878 (M^+, 0.05), 877 ($M^+ - 1$, 0.6), 863 ($M^+ - 15$, 0.2), 745 ($M^+ - (C_4H_9–C_6H_4)$), 567 (11), 566 (45), 565 ($M^+ - (C_4H_9–C_6H_4)_2PO$, 100), 317 (5.3), 313 (3.5), 299 (2.4), 297 (2.3); HRMS (70 eV), *m/z* 878.4357, calcd for $C_{60}H_{64}O_2P_2$ 878.4380. Other spectral data of **5** were recorded for (*S*)-(–)-**5**.

Optical Resolution of (±)-5. The following experimental conditions for the optical resolution was not fully optimized. To a boiling solution of (±)-**5** (6.15 g, 7.00 mmol) in chloroform (300 mL) was added a solution of (2*R*,3*R*)-(–)-2,3-*O*-dibenzoyltartaric acid monohydrate ((–)-**7** monohydrate) (2.65 g, 7.04 mmol) in ethyl acetate (250 mL). The mixture was allowed to stand at room temperature for 24 h. The white precipitates were separated by filtration and recrystallized 3 times from a mixture of chloroform and ethyl acetate to give 1.70 g (39% based on the (*S*)-(–)-**5** used) of essentially pure 1:1 complex of (*S*)-(–)-**5** and (–)-**7**, mp 187–189 °C dec, $[\alpha]^{24}_D$ –86° (*c* 1.1, chloroform). The complex obtained

above was treated with 0.5 N NaOH solution (80 mL) and extracted with three 50-mL portions of chloroform. The combined chloroform layer was washed with water (100 mL) and dried over Na_2SO_4. Evaporation of the solvent gave (*S*)-(−)-**5** (1.11 g, 36% based on the initially used (*S*)-(−)-**5**), mp 225–232 °C, $[\alpha]^{24}_D$ −107° (*c* 1.1, chloroform). (*S*)-(−)-**5**: ^{1}H NMR ($CDCl_3$) δ 1.19 (s, 6 CH_3), 1.37 (s, 6 CH_3), 6.50 (d, 2 H, *J* = 7.9 Hz), 6.92 (t, 2 H, *J* = 7.0 Hz), 6.96–7.03 (m, 4 H), 7.06–7.14 (dd, 4 H, *J* = 7.6 and 12.5 Hz), 7.33–7.40 (m, 2 H), 7.44–7.53 (dd, 2 H, *J* = 8.6 and 13.1 Hz), 7.61–7.67 (m, 4 H), 7.75–7.84 (m, 6 H), 7.97 (d, 2 H, *J* = 7.0 Hz); ^{31}P NMR ($CDCl_3$) 29.5 ppm; IR (KBr) ν 3050 (m), 2950 (s), 2900 (m), 2870 (m), 1598 (m), 1553 (w), 1502 (m), 1462 (m), 1392 (m), 1363 (m), 1302 (w), 1265 (m), 1195 (s), 1133 (m), 1112 (w), 1018 (w), 869 (w), 815 (m), 810 (m), 751 (s), 740 (m), 693 (w), 683 (w), 650 (m), 607 (s), 581 (w), 568 (w), 557 (m), 522 (m), 489 (m) cm^{-1}; UV (ethanol) λ_{max} 233 (ε 130 000), 273 (sh, 12 000), 287 (12 000), 300 (sh, 10 000), 316 (sh, 3600), 332 (3500) nm.

The purification of the antipode (*R*)-(+)-**5**, which went to the mother liquor of recrystallization of the (*S*)-(−)-**5**–(−)-**7** complex was not carried out.

Reduction of (*S*)-(−)-5 into 2,2′-Bis[bis(*p*-*tert*-butylphenyl)phosphinyl]-1,1′-binaphthyl [*p*-*tert*-BuC$_6$H$_4$BINAP] [(*S*)-(−)-9]. To a mixture of (*S*)-(−)-**5** (1.50 g, 1.71 mmol) and triethylamine (1.65 mL, 1.20 g, 11.9 mmol) in xylene (25 mL) was added dropwise a solution of trichlorosilane (1.40 g, 10.3 mmol) in xylene (5 mL) at 20 °C. After the addition was completed, the mixture was heated with stirring at 100–110 °C for 3 h. Workup as described above gave 0.75 g (52%) of (*S*)-(−)-**9**, mp 263–265 °C, $[\alpha]^{24}_D$ −83° (*c* 1.0, benzene). (*S*)-(−)-**9**: ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 6 CH_3), 1.26 (s, 6 CH_3), 6.65 (d, 2 H, *J* = 8.5 Hz), 6.74 (t, with fine splitting, 2 H, *J* = 7.6 Hz), 6.92–6.98 (m, 4 H), 7.06 (d, 4 H, *J* = 7.9 Hz), 7.08–7.16 (m, 4 H), 7.20–7.32 (m, 6 H), 7.47 (d, with fine splitting, 2 H, *J* = 7.0 Hz), 7.78 (d, 2 H, *J* = 8.2 Hz), 7.87 (d, 2 H, *J* = 8.2 Hz); ^{31}P NMR ($CDCl_3$) −16.4 ppm; IR (KBr) ν 3050 (w), 2950 (s), 2895 (w), 2860 (w), 1596 (w), 1551 (w), 1495 (m), 1461 (m), 1392 (m), 1361 (m), 1307 (w), 1264 (s), 1200 (w), 1082 (s), 1015 (s), 946 (w), 865 (w), 825 (s), 815 (s), 776 (w), 745 (s), 697 (w), 645 (w), 581 (w), 556 (m), 515 (w), 456 (w), cm^{-1}; LRMS (70 eV), *m*/*z* (% intensity) 846 (M^+, 0.14), 552 (11), 551 (48), 550 (100), 549 (M^+ − (C_4H_9–C_6H_4)$_2$P, 1.3), 298 ((C_4H_9–C_6H_4)$_2$P, 2.3); HRMS (70 eV), *m*/*z* 846.4464, calcd for $C_{60}H_{64}P_2$ 846.4482. UV (ethanol) λ_{max} 221 (ε 125 000), 237 (sh, 100 000) nm. Anal. Calcd for $C_{60}H_{64}P_2$: C, 85.07; H, 7.62. Found: C, 84.95; H, 8.03.

X-ray Analysis of the Complex of (*S*)-(−)-3, (1*R*)-(−)-6, and Acetic Acid. Crystal data for the title complex are given in Table I. Single crystals were grown from a solution of the complex (0.25 g, 0.38 mmol) in a mixture of ethyl acetate (8.5 mL) and acetic acid (0.1 mL). A suitable crystal was sealed in a thin-walled glass capillary. Diffraction data were collected with graphite-monochromated Cu Kα radiation. Fifty accurately centered reflections in the range 40° < 2θ < 60° were used for determination and least-squares refinement of the unit cell parameters. A total of 8589 reflections were collected and 7842 reflections had $|F_o| > 3\sigma(F_o)$, in which 5062 are independent. Three standard reflections, measured after every 50 reflections, showed neither indication of any misalignment nor deterioration of the crystal. The intensities were empirically corrected for Lorents and polarization factors and used in the structure determination. The structure solution by the use of the direct method (MULTAN 78 program) for 5062 reflections revealed positions for 48 non-hydrogen atoms, containing two phosphorus atoms. Three cycles of blockdiagonal least-squares refinement converged to $R = 0.27$ and $R_w = 0.34$. The remaining non-hydrogen atoms and hydrogen atoms were located after carrying out a series of blockdiagonal least-squares refinement and Fourier and difference Fourier syntheses. Total 123 atoms were refined by use of anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms. Least-squares refinement based on 7842 observed reflections led to a final $R = 5.96\%$ and $R_w = 7.08\%$. The bond parameters in crystal solvent ethyl acetate have fairly large estimated standard deviations as is often observed for solvate molecules. Ten hydrogen atoms were not located from final difference Fourier maps. Selected bond lengths and angles appear in Table II. Coordinates and thermal parameters for 123 atoms, observed and calculated structure factor amplitudes, all bond lengths and angles, and best planes (14 pages) are included as supplementary material.

Acknowledgment. We thank Dr. C. Katayama, Nagoya University, for valuable contribution in X-ray crystal structure analysis. We gratefully acknowledge financial support from the Ministry of Education, Science, and Culture, Japan (No. 59540331 and 60219012).

Supplementary Material Available: Lists of atomic coordinates, thermal parameters, bond distances, bond angles, and best planes (14 pages). Ordering information is given on any current masthead page.

Approach to the Total Synthesis of Chlorothricolide: Synthesis of (±)-19,20-Dihydro-24-*O*-methylchlorothricolide, Methyl Ester, Ethyl Carbonate†[1]

Robert E. Ireland* and Michael D. Varney[2]

The Chemical Laboratories, California Institute of Technology, Pasadena, California 91125

Received September 3, 1985

An approach to the total synthesis of the macrolide antibiotic aglycone chlorothricolide (**1b**) is presented. Herein is described the synthesis of the advanced intermediate (±)-19,20-dihydro-24-*O*-methylchlorothricolide, methyl ester, ethyl carbonate (**34**) from the "bottom half" acid **4** and the "top half" alcohol **3** by the sequence esterification, macrolactonization, ester enolate Claisen rearrangement, and decarboxylation.

Chlorothricin (**1a**), one of some 500 known macrolide antibiotics,[3] was isolated in 1969 by W. Keller-Schierlein.[4] Active against gram-positive bacteria, it functions as a noncompetitive inhibitor of pyruvate carboxylase.[5] The aglycone chlorothricolide methyl ester (**1b**) has been the subject of intense study by many synthetic chemists in recent years.[6] In previous reports[6a,b] from this group, a convergent synthetic strategy was presented for the construction of chlorothricolide (**1b**). Central to the proposal was the joining of two nearly equal halves along the C12–

† Contribution No. 7249.

(1) Grateful acknowledgment is made for support of this investigation by a grant from NSF (CHE-82-03494). Acknowledgment is also made for the use of the Southern California Regional NMR Facility (National Science Foundation Grant No. CHE-79-16324) and for use of the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE (National Science Foundation Regional Instrumentation Facility) for all high-resolution mass spectra.

(2) Atlantic Richfield Foundation Research Fellow, 1984.

0022-3263/86/1951-0635$01.50/0